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Aug 22, 2002

DERWENT-ACC-NO: 2002-643481

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TITLE: New tyrosine kinase polypeptide and polynucleotide, useful for preventing, ameliorating or treating diseases associated with tyrosine kinase dysfunction, e.g. cancer

INVENTOR: SMITH, J T

PATENT-ASSIGNEE:

ASSIGNEE

CODE

BAYER AG

FARB

PRIORITY-DATA: 2001US-331475P (November 16, 2001), 2001US-267656P (February 12, 2001)

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PATENT-FAMILY:

| PUB-NO | PUB-DATE | LANGUAGE | PAGES | MAIN-IPC |
|---|------------------|----------|-------|------------|
| <input type="checkbox"/> WO 200264762 A2 | August 22, 2002 | E | 123 | C12N009/00 |
| <input type="checkbox"/> AU 2002250911 A1 | August 28, 2002 | | 000 | C12N009/00 |
| <input type="checkbox"/> AU 2002250911 A8 | October 20, 2005 | | 000 | C07K016/40 |

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

APPLICATION-DATA:

| PUB-NO | APPL-DATE | APPL-NO | DESCRIPTOR |
|----------------|-------------------|------------------------------|------------|
| WO 200264762A2 | February 11, 2002 | 2002WO-EP01393 | |
| AU2002250911A1 | February 11, 2002 | 2002AU-0250911 | |
| AU2002250911A1 | | WO 200264762 | Based on |
| AU2002250911A8 | February 11, 2002 | 2002AU-0250911 | |
| AU2002250911A8 | | WO 200264762 | Based on |

INT-CL (IPC): C07K 16/40; C12N 9/00; C12N 9/16

ABSTRACTED-PUB-NO: WO 200264762A

BASIC-ABSTRACT:

NOVELTY - A new isolated polynucleotide (I) selected from a polynucleotide which encodes a tyrosine kinase polypeptide (II).

DETAILED DESCRIPTION - A new isolated polynucleotide (I) selected from a polynucleotide:

- (i) which encodes a tyrosine kinase polypeptide (II);
- (ii) which comprises a sequence of 1059 or 2495 base pairs (bp) given in the specification;
- (iii) which hybridizes under stringent conditions to the polynucleotide in (i) and (ii), and encodes (II);
- (iv) which has a sequence deviating from (i)-(iii) due to the degeneration of the genetic code, and which encodes (II); and
- (v) which represents a fragment, derivative or allelic variation of (i)-(iv), and which encodes (II).

The tyrosine kinase polypeptide comprises a sequence (S1) of 352 or 568 amino acids fully defined in the specification, or a sequence that is at least 60% identical to (S1).

INDEPENDENT CLAIMS are also included for the following:

- (1) an expression vector containing the above polynucleotide;
- (2) a host cell comprising the expression vector;
- (3) a substantially purified tyrosine kinase polypeptide encoded by (I);
- (4) methods for producing (II);
- (5) methods for detecting (I) or the polypeptide;
- (6) a diagnostic kit for conducting method (5);
- (7) methods of screening for agents which modulate or decrease the activity of a tyrosine kinase;
- (8) methods of reducing the activity of tyrosine kinase;
- (9) a reagent that modulates the activity of a tyrosine kinase polypeptide or polynucleotide, which is identified by method (7);
- (10) a pharmaceutical composition comprising the above reagent or a reagent which specifically binds to a polypeptide comprising (S1) or to a product of the polynucleotide, the expression vector cited above, and a carrier;
- (11) a cDNA encoding the above polypeptide;
- (12) a fusion protein comprising (II);
- (13) a method of detecting a coding sequence of the above polypeptide;
- (14) a kit for conducting method (13) comprising a polynucleotide having 11

contiguous nucleotides of a sequence comprising 1059 or 2495 bp fully defined in the specification or an antibody which specifically binds to the polypeptide, and instructions for use; and

(15) a method of treating a tyrosine kinase dysfunction-related disease, particularly cancer.

ACTIVITY - Cytostatic. A sequence of 24 bases complementary to the nucleotides at position 1-24 of a sequence with 1059 base pairs (bp) was used as the test oligonucleotide. As control, another sequence was used: 5'-TCA ACT GAC TAG ATG TAC ATG GAC-3'. The oligonucleotides were ethanol-precipitated and suspended in phosphate buffered saline, then its purity was tested. The purified oligonucleotides were added to the culture medium at 10 micro M once a day for 7 days. The addition of test oligonucleotide resulted in reduced expression of the tyrosine kinase. This effect was not observed with the control oligonucleotide. The number of cells in cultures treated with the test oligonucleotide was not more than 30% of control, indicating that the inhibition of human tyrosine kinase had an anti-proliferative effect on cancer cells.

MECHANISM OF ACTION - Gene therapy; Tyrosine-Kinase-Inhibitor; Tyrosine-Kinase-Stimulator.

USE - The polynucleotide and polypeptide are useful in preventing, ameliorating, or treating diseases associated with tyrosine kinase dysfunction, such as cancer. The tyrosine kinase is also useful in diagnostic assays or in genetic testing. The expression vector or the reagent is useful in the preparation of a medicament for modulating the activity of tyrosine kinase in a disease such as cancer (claimed). The fusion protein is useful for generating antibodies against the polypeptide amino acid sequences and for use in various assay systems. The polynucleotide may also be used as hybridization probes or primers, and in identifying and expressing the cDNAs. The methods are useful in producing and detecting the polynucleotide and polypeptide and in screening for agents that modulate the activity of the tyrosine kinase.

CHOSEN-DRAWING: Dwg.0/17

TITLE-TERMS: NEW TYROSINE KINASE POLYPEPTIDE POLYNUCLEOTIDE USEFUL PREVENT AMELIORATE TREAT DISEASE ASSOCIATE TYROSINE KINASE DYSFUNCTION CANCER

DERWENT-CLASS: B04 D16

CPI-CODES: B04-B03C; B04-E03E; B04-E03F; B04-E06; B04-E07; B04-E08; B04-F0100E; B04-G01; B04-L0400E; B04-M01; B04-N04A; B04-N04A0E; B04-N08; B11-C08E; B11-C08E5; B11-C10; B12-K04E; B12-K04F; B14-H01; B14-S03A; D05-H09; D05-H10; D05-H11; D05-H12A; D05-H12D2; D05-H12D4; D05-H14; D05-H17A3; D05-H17A6; D05-H18;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
Fragmentation Code
M423 M424 M710 M740 M750 M781 M905 N102 N135 P616
P633 P831 Q233 Q505
Specific Compounds
A00NST A00NSA A00NSD A00NSN

Chemical Indexing M1 *02*
Fragmentation Code
M423 M424 M710 M740 M750 M781 M905 N102 N135 P616
P633 P831 Q233 Q505

Specific Compounds
A012PT A012PA A012PD A012PN

Chemical Indexing M1 *03*
Fragmentation Code
M417 M423 M710 M905 N135 N136 Q233
Specific Compounds
A00GTN

Chemical Indexing M1 *04*
Fragmentation Code
M417 M423 M424 M710 M720 M740 M750 M781 M905 N102
N135 N136 N161 P616 P633 P831 Q233 Q505
Specific Compounds
A00GCT A00GCA A00GCD A00GCN A00GCP

Chemical Indexing M1 *05*
Fragmentation Code
M417 M423 M424 M710 M720 M740 M750 M781 M905 N102
N135 N136 N161 P616 P633 P831 Q233 Q505
Specific Compounds
A00H1T A00H1A A00H1D A00H1N A00H1P

Chemical Indexing M1 *06*
Fragmentation Code
M417 M423 M424 M710 M720 M740 M750 M781 M905 N102
N135 N136 N161 P616 P633 P831 Q233 Q505
Specific Compounds
A00H3T A00H3A A00H3D A00H3N A00H3P

Chemical Indexing M1 *07*
Fragmentation Code
M417 M423 M710 M781 M905 P616 P633 Q233
Specific Compounds
A00C8T A00C8N A00C8U

Chemical Indexing M1 *08*
Fragmentation Code
M417 M423 M710 M781 M905 P616 P633 Q233
Specific Compounds
A013IT A013IN A013IU

Chemical Indexing M1 *09*
Fragmentation Code
M423 M710 M781 M905 P616 P633 Q233
Specific Compounds
A6URBT A6URBN A6URBU

Chemical Indexing M6 *10*
Fragmentation Code
M905 P616 P633 P831 Q233 Q505 R515 R521 R614 R624
R627 R632 R633 R637 R639

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C2007-013327

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